



SHEET 1 OF 7

## Form PTO - 1449 (Modified)

FORM PTO-1449 U.S. DEPARTMENT OF COMMERCE  
(Modified) PATENT AND TRADEMARK OFFICE

ATTY. DOCKET NO.

4952.US.C1

SERIAL NO.

09/735,056

INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT

(Use several sheets if necessary)

APPLICANT(S)

L. Katz, et al.

FILING DATE

December 11, 2000

GROUP

1652

(37 CFR 1.98 (b))

## U.S. PATENT DOCUMENTS

EXAMINER INITIAL		PATENT NUMBER	ISSUE DATE	INVENTOR	CLASS	SUB CLASS	FILING DATE
WWM	A1	4,874,748	10-17-89	Katz, et al.	514	29	
WWM	A2	4,921,801	05-01-90	Rao, et al.	435	474	
WWM	A3	4,935,340	06-19-90	Baltz, et al.	435	6	
WWM	A4	5,081,023	01-14-92	Yaginuma, et al.	435	76	
WWM	A5	5,087,563	02-11-92	Beremand, et al.	435	69.7	
WWM	A6	5,110,728	05-05-92	Kridl, et al.	435	69.1	

## FOREIGN PATENT OR PUBLISHED FOREIGN PATENT APPLICATION

		DOCUMENT NUMBER	PUBLIC- ATION DATE	COUNTRY OR PATENT OFFICE	CLASS	SUB CLASS	TRANS- LATION YES NO
WWM	B1	EP 0 204 549 A2	12-10-86	EPO			
WWM	B2	EP 0 238 323 A2	09-23-87	EPO			
WWM	B3	WO 93/13663	06-22-93	WIPO			
WWM	B4	WO 96/40968	12-19-96	WIPO			

## OTHER DOCUMENTS (Including Author, Title, Date, Place of Publication)

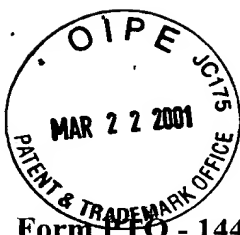
WWM	C1	Aigle, et al., <i>Microbiology</i> , An Amplifiable and Delectable Locus of <i>Streptomyces Ambofaciens</i> RPT81110 Contains a Very Large Gene Homologous to Polyketide Synthase Genes, 142:2815-2824 (1996)
WWM	C2	Aparicio, et al., <i>Gene</i> , Organization of the Biosynthetic Gene Cluster for Rapamycin in <i>Streptomyces Hygroscopicus</i> : Analysis of the Enzymatic Domains in the Modular Polyketide Synthase, 169:9-16 (1996)
WWM	C3	Aparicio, et al., <i>The Journal of Biochemical Chemistry</i> , Limited Proteolysis and Active-Site Studies of the First Multienzyme Component of the Erythromycin-Producing Polyketide Synthase, 269:8524-8528 (1994)
WWM	C4	Ashworth, et al., <i>J. Chem. Soc. Perkin Trans.</i> , On the Biosynthetic Origins of the Hydrogen Atoms in the Macrotetrolide Antibiotics: and Their Mode of Assembly Catalysed by a Nonactin Polyketide Synthase, I:1461-1467 (1989)
WWM	C5	Baltz, et al., <i>Ann. Rev. Microbiol.</i> , Genetics of <i>Streptomyces Fradiae</i> and Tylosin Biosynthesis, 42:547-574 (1988)
WWM	C6	Bibb, et al., <i>The EMBO Journal</i> , Analysis of the Nucleotide Sequence of the <i>Streptomyces Glaucescens</i> <i>tcml</i> Genes Provides Key Information about the Enzymology of Polyketide Antibiotic Biosynthesis, 8:2727-2736 (1989)

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WWM	A7	5,141,926	08-25-92	Weber, et al.	514	29	
WWM	A8	5,252,474	10-12-93	Gerwain, et al.	435	91.1	
WWM	A9	5,672,491	09-30-97	Khosla, et al.	435	148	
WWM	A10	5,712,146	01-27-98	Khosla, et al.	435	252.35	
WWM	A11	5,744,350	04-28-98	Vinci, et al.	435	254.11	
WWM	A12	5,801,032	09-01-98	Stassi, et al.	435	6	

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WWM	B5	WO 97/06266	02-20-97	WIPO	—	—		
WWM	B6	WO 97/02358	01-23-97	WIPO	—	—		
WWM	B7	WO 98/01546	01-15-98	WIPO	—	—		
WWM	B8	WO 98/01571	01-15-98	WIPO	—	—		

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WWM	C7	Brown, et al., <i>J. Chem. Soc. Chem. Commun.</i> , A Mutant Generated by Expression of an Engineered DEBS1 Protein from the Erythromycin-Producing Polyketide Synthase (PKS) in Streptomyces Coelicolor Produces the Triketide as a Lactone, but the Major Product is the Nor-Analogue Derived from Acetate as Starter Acid, 15:1517-1518 (1995)
WWM	C8	Caffrey, et al., <i>FEBS Letters</i> , Identification of DEBS 1, DEBS 2 and DEBS 3, the Multienzyme Polypeptides of the Erythromycin-Producing Polyketide Synthase from Saccharopolyspora Erythraea, 304:225, 228 (1992)
WWM	C9	Cane, et al., <i>American Chemical Society</i> , Macrolide Biosynthesis 4 Intact Incorporation of a Chain-Elongation Intermediate into Erythromycin, 109: 1255-1257 (1987)
WWM	C10	Cortes, et al., <i>Nature</i> , An Unusually Large Multifunctional Polypeptide in the Erythromycin-Producing Polyketide Synthase of Saccharopolyspora Erythraea, 348:176-178 (1990)
WWM	C11	Cortes, et al., <i>Nature</i> , Repositioning of a Domain in a Modular Polyketide Synthase to Promote Specific Chain Cleavage, 268:1487-1490 (1995)

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Wum	C12	Dhillon, et al., <u>Molecular Microbiology</u> , <i>Molecular Characterization of a Gene from Saccharopolyspora Erythraea (Streptomyces-Erythraeus) which is Involved in Erythromycin Biosynthesis</i> , 3(10):1405-1414 (1989)
Wum	C13	Donadio, et al., <u>Gene</u> , <i>Organization of the Enzymatic Domains in the Multifunctional Polyketide Synthase Involved in Erythromycin Formation in Saccharopolyspora Erythraea</i> , 111:51-60 (1992)
Wum	C14	Donadio, et al., <u>Gene</u> , <i>Biosynthesis of the Erythromycin Macrolactone and a Rational Approach for Producing Hybrid Macrolides</i> , 115:97-103 (1992)
Wum	C15	Donadio, et al., <u>Science</u> , <i>Modular Organization of Genes Required for Complex Polyketide Biosynthesis</i> , 252:675-679 (1991)
Wum	C16	Donadio, et al., <u>Genetics and Molecular Biology of Industrial Microorganisms</u> , <i>Genetic Studies on Erythromycin Biosynthesis in Saccharopolyspora Erythraea</i> , 53-59 (1989)
Wum	C17	Fernandez-Moreno, et al., <u>The Journal of Biological Chemistry</u> , <i>DNA Sequence and Functions of the actVI Region of the Actinorhodin Biosynthetic Gene Cluster of Streptomyces Coelicolor A3(2)</i> , 269:24854-24863 (1994)
Wum	C18	Han, et al., <u>Microbiology</u> , <i>Cloning and Characterization of Polyketide Synthase Genes for Jadomycin B Biosynthesis in Streptomyces Venezuelae ISP5230</i> , 140:3379-3389 (1994)
Wum	C19	Harris, et al., <u>The Practical Approach Series</u> , <i>Protein Purification Methods</i> , 56-67 (1989)
Wum	C20	Haydock, et al., <u>FEBS Letters</u> , <i>Divergent Sequence Motifs Correlated with the Substrate Specificity of (Methyl) Malonyl-CoA: Acyl Carrier Protein Transacylase Domains in Modular Polyketide Synthesis</i> , 374:246-248 (1995)
Wum	C21	Haydock, et al., <u>Mol. Gen. Genet.</u> , <i>Cloning and Sequence Analysis of Genes Involved in Erythromycin Biosynthesis in Saccharopolyspora Erythraea: Sequence Similarities Between EryG and a Family of S-Adenosylmethionine-Dependent Methyltransferases</i> , 230:120-128 (1991)
Wum	C22	Hopwood, et al., <u>GIM 90</u> , <i>Hybrid Pathways for the Production of Secondary Metabolites</i> , Vol. 1:259-270 (1990)
Wum	C23	Hopwood, et al., <u>Ann. Rev. Genet.</u> , <i>Molecular Genetics of Polyketides and Its Comparison to Fatty Acid Biosynthesis</i> , 24:37-66 (1990)

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Wum	C24	Hopwood, et al., <u>Nature</u> , <i>Production of Hybrid Antibiotics by Genetic Engineering</i> , 314:642-644 (1985)
Wum	C25	Hu, et al., <u>Microbiology</u> , <i>Repeated Polyketide Synthase Modules Involved in the Biosynthesis of a Heptaene Macrolide by Streptomyces sp. FR-008</i> , 14(1):163-172 (1994)
Wum	C26	Huber, et al., <u>Antimicrobial Agents and Chemotherapy</u> , <i>Branched-Chain Fatty Acids Produced by Mutants of Streptomyces Fradiae, Putative Precursors of the Lactone Ring of Tylosin</i> , 34:1535-1541 (1990)
Wum	C27	Hutchinson, et al., <u>Annu. Rev. Microbiol.</u> , <i>Polyketide Synthase Gene Manipulation: A Structure-Function Approach in Engineering Novel Antibiotics</i> , 49:201-238 (1995)
Wum	C28	Kakinuma, et al., <u>Tetrahedron</u> , <i>Genetic Studies of the Biosynthesis of Kalafungin, a Benzoisochromanquinone Antibiotic</i> , 31:6059-6068 (1991)
Wum	C29	Kao, et al., <u>Science</u> , <i>Engineered Biosynthesis of a Complete Macrolactone in a Heterologous Host</i> , 265:509-512 (1994)
Wum	C30	Kao, et al., <u>J. Am. Chem. Soc.</u> , <i>Engineered Biosynthesis of a Triketide Lactone from an Incomplete Modular Polyketide Synthase</i> , 116:11612-11613 (1994)
Wum	C31	Kao, et al., <u>Journal of Am. Chem. Soc.</u> , <i>Manipulation of Macrolide Ring Size by Directed Mutagenesis of a Modular Polyketide Synthase</i> , 117:9105-9106 (1995)
Wum	C32	Kao, et al., <u>Biochemistry</u> , <i>Evidence for Two Catalytically Independent Clusters of Active Sites in a Functional Modular Polyketide Synthase</i> , 35:12363-12368 (1996)
Wum	C33	Kim, et al., <u>Journal of Bacteriology</u> , <i>Heterologous Expression of an Engineered Biosynthetic Pathway: Functional Dissection of Type II Polyketide Synthase Components in Streptomyces Species</i> , 177:1202-1207 (1995)
Wum	C34	Kinoshita, et al., <u>J. Chem. Soc. Chem. Commun.</u> , <i>Isolation of Proposed Intermediates in the Biosynthesis of Mycinamicins</i> , 943-945 (1988)
Wum	C35	Kirst, et al., <u>Antimicrobial Agents and Chemotherapy</u> , <i>New Directions for Macrolide Antibiotics: Structural Modifications and in Vitro Activity</i> , 33:1413-1418 (1989)

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23 September 2002

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WUM	C36	Kuhstoss, et al., <i>Gene</i> , <i>Production of a Novel Polyketide Through the Construction of a Hybrid Polyketide Synthase</i> , 183:231-236 (1996)
WUM	C37	Leadlay, et al., <i>Biochemical Society Transactions</i> , <i>The Erythromycin-Producing Polyketide Synthase</i> , 21:218-221 (1993)
	C38	Li, et al., <i>Chinese Journal of Biotechnology</i> , <i>Cloning and Expression of Spiramycin Polyketide Synthase Genes and Resistance Genes from S. Spiramyceticus U-1941</i> , 7:33-42
WUM	C39	MacNeil, et al., <i>Annals of the New York Academy of Sciences</i> , <i>Correlation of the Avermectin Polyketide Synthase Genes to the Avermectin Structure</i> , 721:123-132 (1994)
WUM	C40	Malpartida, et al., <i>Nature</i> , <i>Homology between Streptomyces Genes Coding for Synthesis of Different Polyketides Used to Clone Antibiotic Biosynthetic Genes</i> , 325:818-821 (1987)
WUM	C41	Marsden, et al., <i>Science</i> , <i>Stereospecific Acyl Transfers on the Erythromycin-Producing Polyketide Synthase</i> , 263:378-380 (1994)
WUM	C42	Motamedi, et al., <i>Euro. J. Biochem.</i> , <i>Structural Organization of a Multifunctional Polyketide Synthase Involved in the Biosynthesis of the Macrolide Immunosuppressant FK506</i> , 244:74-80 (1997)
	C43	Motamedi, et al., <i>Merck Research Laboratories</i> , <i>FK506 Polyketide Synthase is a Large Multifunctional Polypeptide with 19 FAS-like Domains</i>
WUM	C44	Oliynyk, et al., <i>Chemistry &amp; Biology</i> , <i>A Hybrid Modular Polyketide Synthase Obtained by Domain Swapping</i> , 3:833-839 (1996)
WUM	C45	Omura, et al., <i>J. Antibiotics</i> , <i>Biosynthetic Origin of Carbons 3 and 4 of Leucomycin Aglycone</i> , 36:611-613 (1983)
WUM	C46	Otten, et al., <i>Journal of Bacteriology</i> , <i>Cloning and Expression of Daunorubicin Biosynthesis Genes From Streptomyces Peucetius and S. Peucetius Subsp. Caesius</i> , 172:3427-3434 (1990)
WUM	C47	Pieper, et al., <i>Nature</i> , <i>Cell-Free Synthesis of Polyketides by Recombinant Erythromycin Polyketide Synthases</i> , 378:263-266 (1995)
WUM	C48	Richardson, et al., <i>Journal of Bacteriology</i> , <i>Cloning of Spiramycin Biosynthetic Genes and Their Use in Constructing Streptomyces Ambofaciens Mutants Defective in Spiramycin Biosynthesis</i> , 173:3790-3798 (1990)

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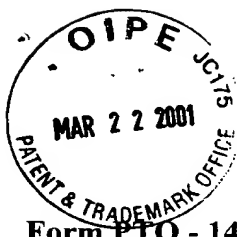
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WWM	C50	Salas, et al., <i>BIOTEC-90</i> , Genetic Manipulation of Antibiotic Biosynthesis by Actinomycetes, 47-52 (1990)
WWM	C51	Schwecke, et al., Proc. Natl. Acad. Sci., The Biosynthetic Gene Cluster for the Polyketide Immunosuppressant Rapamycin, 92:7839-7843 (1995)
WWM	C52	Sherman, et al., The EMBO Journal, Structure and Deduced Function of the Granaticin-Producing Polyketide Synthase Gene Cluster of Streptomyces Violaceoruber Tu22, 8:2717-2725 (1989)
WWM	C53	Stanzak, et al., BIO/Technology, Cloning and Expression in Streptomyces Lividans of Clustered Erythromycin Biosynthesis Genes from Streptomyces Erythreus, 4:229-232 (1986)
WWM	C54	Stassi, et al., Journal of Bacteriology, Identification of a Saccharopolyspora Erythraea Gene Required for the Final Hydroxylation Step in Erythromycin Biosynthesis, 175:182-189 (1993)
WWM	C55	Staunton, et al., Nature Structural Biology, Evidence for a Double-Helical Structure for Modular Polyketide Synthases, 3:188-192 (1996)
WWM	C56	Summers, et al., Biochemistry, Malonyl-Coenzyme A:Acyl Carrier Protein Acyltransferase of Streptomyces Glaucescens: A Possible Link Between Fatty Acid and Polyketide Biosynthesis, 34:9389-9402 (1995)
WWM	C57	Swan, et al., Mol. Gen Genet, Characterization of a Streptomyces Antibioticus Gene Encoding a Type I Polyketide Synthase which has an Unusual Coding Sequence, 242:358-362 (1994)
WWM	C58	Tomich, Antimicrobial Agents and Chemotherapy, Streptomyces Cloning: Possible Construction of Novel Compounds and Regulation of Antibiotic Biosynthetic Genes, 32:1472-1476 (1988)
WWM	C59	Tuan, et al., Gene, Cloning of Genes Involved in Erythromycin Biosynthesis from Saccharopolyspora Erythraea using a Novel Actinomycete-Escherichia Coli Cosmid, 90:21-29 (1990)
WWM	C60	Vara, et al., Journal of Bacteriology, Cloning of Genes Governing the Deoxysugar Portion of the Erythromycin Biosynthesis Pathway in Saccharopolyspora Erythraea (Streptomyces Erythreus), 171:5872-5881 (1989)

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Wm	C62	Weber, et al., <u>Journal of Bacteriology</u> , Organization of a Cluster of Erythromycin Genes in Saccharopolyspora Erythraea, 172:2372-2383 (1990)
Wm	C63	Weber, et al., <u>Science</u> , An Erythromycin Derivative Produced by Targeted Gene Disruption in Saccharopolyspora Erythraea, 252:114-117 (1991)
Wm	C64	Wiesmann, et al., <u>Chemistry &amp; Biology</u> , Polyketide Synthesis In Vitro on a Modular Polyketide Synthase, 2:583-589 (1995)

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